

AMENDMENT

In the Claims:

Please replace the presently pending claims with the following claims:

23. A hybrid modular polyketide synthase (PKS) comprising at least a first naturally occurring extender module and a second naturally occurring extender module of a different PKS from said first module,

wherein the C-terminus of said first module is covalently linked to the N-terminus of a naturally occurring intra-molecular linker (RAL) or inter-molecular linker (ERL) and the N-terminus of the second module is covalently linked to the C-terminus of said RAL or ERL, and

wherein either said first module or second module is not covalently linked to said RAL or ERL in a naturally occurring polyketide synthase;

whereby the transfer of a nascent polyketide chain from said first module to said second module is facilitated.

25. The hybrid modular PKS of claim 23 wherein said RAL is selected from the group consisting of M2 *ery*, M4 *ery*, M6 *ery*, M2 *rif*, M3 *rif*, M5 *rif*, M3 *rap*, M4 *rap*, and M7 *rap* intra-module linkers (SEQ. ID. NO's: 3-11, respectively).

C¹ 26. (Twice amended) The hybrid modular PKS of claim 23 wherein the portion of the ERL at the N-terminus of the second module is selected from the group consisting of SEQ. ID. NO's: 12-19, respectively.

28. (Twice amended) The hybrid modular PKS of claim 23 which contains *ery* modules 1 and 3 through 6 inclusive and tylosin module 2, and wherein said polyketide chain is transferred from *ery* module 1 to *tyl* module 2 and then to *ery* modules 3 through 6 inclusive.

C² 29. (Twice amended) The hybrid modular PKS of claim 23 which contains *ery* modules 1 through 5 inclusive and narbomycin module 6, wherein said polyketide chain is transferred from *ery* modules 1 through 5 inclusive to *nar* module 6.

30. (Twice amended) The hybrid modular PKS of claim 23 which contains modules 1 and 3 through 6 inclusive of *ery* and modules 2-3 of tylosin, spiramycin or niddamycin, wherein said polyketide chain is transferred from *ery* module 1 to modules 2-3 of tylosin, spiramycin or niddamycin and then to *ery* modules 3 through 6 inclusive.

31. (Twice amended) The hybrid modular PKS of claim 23 which contains modules 1 through 3 inclusive of tylosin, spiramycin or niddamycin and modules 3 through 6 inclusive of *ery*, and wherein said polyketide chain is transferred from modules 1 through 3 inclusive of said tylosin, spiramycin or niddamycin to *ery* modules 3 through 6 inclusive.

32. (Twice amended) The hybrid modular PKS of claim 23 which contains a module of tylosin, spiramycin or niddamycin and modules 1-2 and 3 through 6 inclusive of *ery*, wherein said polyketide chain is transferred from *ery* modules 1-2 to the tylosin, spiramycin or niddamycin module and then to *ery* modules 3 through 6 inclusive.

33. (Twice amended) The hybrid modular PKS of claim 23 which contains modules 1 and 3 through 6 inclusive of *ery* and module 5 of tylosin, spiramycin or niddamycin having the enoyl reductase catalytic activity inactivated, wherein said polyketide chain is transferred from *ery* module 1 to module 5 of tylosin, spiramycin or niddamycin and then to *ery* modules 3 through 6 inclusive.

34. (Twice amended) The hybrid modular PKS of claim 23 which contains *ery* modules 1 through 4 inclusive and 6 and module 6 of spiramycin or niddamycin, wherein said polyketide chain is transferred from *ery* modules 1 through 4 inclusive to module 6 of spiramycin or niddamycin and then to *ery* module 6.

35. (Twice amended) The hybrid modular PKS of claim 23 which contains module 1 of FK-506 or 520 and modules 2 through 14 inclusive of rapamycin, wherein said polyketide chain is transferred from module 1 of FK-506 or 520 and then to modules 2 through 14 inclusive of rapamycin.

36. (Twice amended) The hybrid modular PKS of claim 23 which contains module 1 and 11 through 14 inclusive of rapamycin and modules 2 through 6 inclusive of FK-506 or 520 wherein said polyketide chain is transferred from module 1 of rapamycin to modules 2 through 6 inclusive of FK-506 or 520 and then to modules 11 through 14 inclusive of rapamycin.

37. (Twice amended) The hybrid modular PKS of claim 23 which contains module 1 of rapamycin, modules 2 through 7 inclusive of FK-506 or 520 and modules 12 through 14 inclusive of rapamycin, wherein said polyketide chain is transferred from module 1 of rapamycin to modules 2 through 7 inclusive of FK-506 or 520 and then to modules 12 through 14 inclusive of rapamycin.

C² 38. (Twice amended) The hybrid modular PKS of claim 23 which contains module 1 of rapamycin, modules 2 through 8 inclusive of FK-506 or 520 and modules 13-14 of rapamycin, wherein said polyketide chain is transferred from module 1 of rapamycin to modules 2 through 8 inclusive of FK-506 or 520 and then to modules 13-14 of rapamycin.

39. (Twice amended) The hybrid modular PKS of claim 23 which contains modules 1 through 10 inclusive of rapamycin and modules 7 through 10 inclusive of FK-506 or 520, wherein said polyketide chain is transferred from modules 1 through 10 inclusive of rapamycin to modules 7 through 10 inclusive of FK-506 or 520.
